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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,479	03/31/2004	David W. Moskowitz	60019190-1038	7392

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BLACKWELL SANDERS LLP
720 OLIVE STREET
SUITE 2400
ST. LOUIS, MO 63101

EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,479	MOSKOWITZ, DAVID W.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 8-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment/arguments, filed 11/1/06, are acknowledged and made of record. Applicant's statement that claim 14 has been amended to correct a typographical error and that no new matter has been added by said amendment is acknowledged and made of record.

Status of the claims

Claims 1-15 are currently pending in this application.

Claims 1-5 and 8-13 are withdrawn for examination purposes for being directed to non-elected subject matter.

Claims 6-7 and 14-15 are presented for examination.

Benefit of Claim of Priority

The effective filing date for the subject matter encompassed by claims 6, 14, and 15 (i.e. treatment of viral infections with angiotensin receptor blocker e.g. angiotensin II receptor blockers such as losartan; treatment of SARS with with angiotensin receptor blocker e.g. angiotensin II receptor blockers such as losartan) is considered to be reasonably supported by US Provisional Application No. 60/465,908. Thus, the effective filing date for instant claims 6, 14, and 15 is considered to be 4/25/03.

Except for SARS, the effective filing date for the subject matter encompassed by claim 7 is considered to be the filing date of the instant application i.e. 3/31/2004.

Response to applicant's arguments/remarks

Scope of enablement rejection under 112, first paragraph (claims 6-7 and 14-15)

Applicant contends that this rejection should be withdrawn because:

1) disclosure clearly defines method of administration (page 49, starting line 16) and range of dosages (page 49, starting line 20);

2) ARBs in general and losartan specifically, are known in the art;

3) the essential limitation in the use of ARBs is a patient's blood pressure tolerance (which is well known and discussed in the specification);

4) while the specific examples disclosed in the specification do not exemplify losartan, a person skilled in the art, given the general nature of the disclosure, would clearly understand that the disclosed examples apply equally to the use of losartan

In response, the rejection is maintained. Applicant asserts that the essential limitation in the use of ARBs is a patient's blood pressure; however, applicant fails to show how the effect on blood pressure relates to the achieving the contemplated anti-viral effects in treating any and all viral infections (see claim 6), or in treating any and all diseases associated with excess angiotensin converting enzyme (see claims 14 and 15; see also specification, page 1, last two paragraphs, and page 49, line 1 to page 67, line 7).

Clearly, the term "for treating viral infections" as recited in instant claim 6, given its broadest reasonable possible interpretation, encompasses any and all coronaviruess and non-coronaviruses. Claim 7 recites a diverse group of viral infections which are related only to the extent that they are caused by viruses, but each represent a distinct

clinical disease; different therapeutic modalities are also employed in managing these distinct diseases. Further, a treatment for one would not be reasonably be expected to be effective in treating another. The term "diseases associated with excess angiotensin converting enzyme" as recited in claims 14 and 15 is very broad, which given its broadest reasonable possible interpretation, encompasses any and all diseases present in a subject with coexisting viral infections, and/or renal disease, and/or hypertension. The specification does not provide any specific guidance to treat viral diseases associated with excess angiotensin converting enzyme wherein no respiratory sequelae is involved.

Henley et al. teaches that no specific treatment exists for SARS (Henley et al. SARS: Lessons learned thus far. The Journal of Family Practice. July, 2003; 52(7): electronic pages 1-4; especially page 2, section entitled "Treat with supportive measures'). Haagmans et al. teach that coronaviruses may cause respiratory, enteric and central nervous system disease in many species, including humans (Haagmans et al. Coronaviruses and their therapy. Antiviral Research. 2006; 71(2-3): 397-403; electronic copy, pages 1-13).

Haagmans et al. also disclose that over 10,000 agents against SARS-CoV in vero cells have been tested, but only 50 were found to be active against SARS-CoV (page 7, last paragraph).

The Merck Manual Home Edition teaches that there is no specific treatment for arbovirus encephalitis or progressive multifocal leukoencephalopathy, or tropical spastic paraparesis (also called HTLV-associated myelopathy) (The Merck Manual

Home Edition. 2003; pages 5-8; already made of record). Furthermore, in the absence of microbiology data that establishes a reasonable correlation between the dose of an ARB and minimum/maximum inhibitory concentrations of said drugs against the multiplicity of the different strains of the various viruses encompassed by the instant application, a artisan skilled in the would not be able to predictably practice the instant claimed invention without conducting undue experimentation. Although the instant invention is enabled for the treatment of coronavirus infections associated with pulmonary symptoms/syndromes (e.g. SARS) comprising administering an angiotensin II converting enzyme inhibitor, the specification does not reasonably provide enablement for treating all viral infections or all diseases associated with excess angiotensin converting enzyme with any and all angiotensin converting enzyme inhibitors.

Kuba et al. disclose that the rennin-angiotensin system (RAS) plays a key role in maintaining blood pressure homeostatsis, as well as fluid and salt balance, and may play a critical role in the pathogenesis of acute lung injury (Kuba et al. Angiotensin-converting enzyme 2 in lung disease. Curr Opin Pharmacol. 2006; 6(3):271-6, abstract only).

Oxford et al. teach that the only currently accepted intervention for treating SARS is interferon (Oxford et al. New antiviral drugs, vaccines and classic public health interventions against SARS coronavirus. 2005; 16(1):13-21, abstract only).

Based on the unpredictability and uncertainty in the art, an artisan skilled in the would have to conduct undue experimentation to reasonably practice the instant

claimed invention commensurate with the scope of the claims. Thus, for the reasons stated above, the rejection is maintained with respect to claims 6, 14 and 15.

Rejection under 102(e) (claims 6-7, and 14-15)

Applicant proffers the following arguments/statements:

1) Olsen (US Patent Application Publication No. 2004/0259934) claims priority to two provisional applications, dated May 1, 2003 and May 15, 2003. Applicant's application at issue claims priority to several provisional applications, including 60/465,908, filed on April 25, 2003. Olsen therefore cannot anticipate the applicant's application since the Olsen publication has a later effective filing date;

2) Examiner cited Olsen teaching regarding SARS treatment, wherein Olsen cited two GenoMed press releases (see 8/2/06 Office action at page 5); Genomed is the assignee of the applicant's application, and these press releases correspond to the provisional application filed by the applicant on April 25, 2003. Since the examiner found these disclosures to be relevant support for the 102 rejection, it cannot now be argued that these disclosures, and the corresponding provisional application, are not relevant to support the applicant's claim priority.

This rejection is withdrawn as applicant's arguments are found to be persuasive.

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-7 and 14-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification and the prior art combined, while being enabling for a method of treating symptoms related to viral infections which is considered an embodiment within the scope of the treatment of coronavirus infections associated with pulmonary symptoms/syndromes (e.g. SARS), does not reasonably provide enablement for the treatment of a viral infection via a treatment that targets the viral agent itself. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2nd 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention

commensurate in scope with theclaims without the need for undue experimentation as evidenced by the above discussion under the Response to applicant's arguments/remarks with respect to the rejection under 112, first paragraph, is incorporated by reference, and for the additional reasons set forth below.

Chobanian et al. (US Patent 5,645,839) teach that once consequence of heart disease is activation of the body's reninangiotensin-aldosterone system (RAAS), which maintains normal fluid volume in the body; the sympathetic nervous system provokes the relase of the renin from the kidneys (col. 2, lines 56-63). Renin is a proteolytic enzyme that acts on angiotensinogen to produce the decapeptide angiotensin I; angiotensin I is then converted to angiotensin II by the action of angiotensin-converting enzyme (ACE) (col. 2, lines 56-67). Angiotensin II is a potent pressor agent producing a rapid elevation in blood pressure and plays a role in proliferation of smooth muscle cells (col. 2, line 67 to col. 4, line 53). Chobanian et al. teach that "angiotensin inhibitor" includes an agent that interferes with the function, synthesis or catabolism of angiotensin II (or A-II) e.g. angiotensin-converting enzyme (ACE) inhibitors; agents that activate the catabolims of (A-II), and agents that prevent the synthesis of angiotensin I from which A-II is ultimately derived (col. 4, lines 36-43).

Schindler et al. teach that administration of ACE inhibitors reduce vascular proliferation following endothelial injury as well as progression of renal disease in various naimal models; these effects may be due to interference with cytokines such as interleukin I (IL-I) or tumour necrosis factor alpha (TNF) since they have been implicated in regulating the effects of vascular cell growth factors (Schindler et al. Angiotensin-

converting-enzyme inhibitors suppress synthesos of tumour necrosis factor and interleukin I by human perippheral blood mononuclear cells. Cytokine. 1995;7(6):526-533; especially, abstract). Ramipril, lisinopril, perindopril and spiraprtil had no significant effect on TNF synthesis suggesting that the effect was not related specifically to the inhibition of ACE (abstract). Schinlder et al. disclose that only certain ACE-inhibitors suppress IL-I and TNF synthesis at a posttranscriptional level and may therefore influence cytokine-mediated cell growth.

For the reasons stated above, claims 6, 14 and 15 are rejected under 112, 1st paragraph, because while the instant invention is enabled for the treatment of coronavirus infections comprising administering an angiotensin II converting enzyme inhibitor, the specification does not reasonably provide enablement for treating any and all viral infections or any and all diseases associated with excess angiotensin converting enzyme with any and all angiotensin converting enzyme inhibitor. This is a scope of enablement rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

19 September 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER